REMARKS

Claims 1 to 16 are pending. Claims 2 to 6 have been canceled. Thus, Claims 1 and 7-16 remain under consideration. Claim 1 is amended.

Amendment to the Claims

Claim 1 has been amended to recite a method of treating basal cell carcinoma in a subject, the method comprising administering to the subject an amount of an IRM compound effective for treating basal cell carcinoma, wherein the IRM compound is administered in a treatment cycle that comprises at least five consecutive days in which the IRM compound is administered and at least two days in which the IRM compound is not administered. The amendment is supported throughout the specification at, for example, page 9, lines 14-17. No new matter is introduced by the amendment.

§ 102 Rejections

Claims 1-16 stand rejected under 35 USC § 102(a) as being anticipated by Shumach *et al.* (*Arch. Dermatol.* 38:1165-1171).

Under 35 USC § 102(a), a claim is anticipated if the claimed subject matter was known or used by others in the U.S., or patented or described in a printed publication in the U.S. or a foreign country before the invention was made by the Applicant. Applicants respectfully traverse the rejection.

Applicants submit that the invention was made prior to the subject matter being known or used in the U.S. or described in a printed publication in the U.S. or a foreign country. In support of this assertion, Applicants' attach the Affidavit of Mary L. Owens, M.D., in which Dr. Owens declares that the subject matter of the claims was invented prior to publication of the Shumach *et al.* reference.

The rejection of claims 1-16 under 35 USC § 102(a) as being anticipated by Shumach *et al.* has been overcome and should be withdrawn.

§ 103 Rejections

Claims 1-12 and 16 stand rejected under 35 USC § 103(a) as being unpatentable over Marks *et al.* or Beutner *et al.* or Kagy *et al.* or Geisse *et al.* Claims 2-6 have been canceled, so that remarks that follow pertain to claims 1, 7-12, and 16. Claim 1 is the lone independent claim. Remarks made below with regard to claim 1 are equally applicable to claims 7-12 and 16.

Each of the cited references is said to teach a method of treating basal cell carcinoma by administering imiquimod 5% cream using varying treatment regimens. The Office Action asserts it would have been *prima facie* obvious to one of ordinary skill in the art to optimize the treatment cycle and arrive at Applicants' invention. Applicants respectfully traverse the rejection.

As an initial matter, Applicants' request that the rejections based on the Marks *et al.* reference and the Geisse *et al.* reference be withdrawn in view of the Affidavit of Mary L. Owens. MPEP § 2141.01 states that an obviousness rejection based on a publication which would be applied under 102(a) if it anticipated the claims can be overcome by swearing behind the publication date of the reference by filing an affidavit or declaration under 37 CFR § 1.131. Exhibits I and II of the Affidavit of Mary L. Owens indicate that the invention was made no later than December 2000, which predates the publication of Marks *et al.* (2002) and Shumach *et al.* (2002).

The Office Action acknowledges that neither Beutner *et al.* nor Kagy *et al.* teach the claimed treatment cycle, amended herein to recite at least five consecutive days of treatment and at least two consecutive days without treatment. The Office Action asserts that the claimed subject matter is merely optimization of the treatment cycle that involves only routine skill in the art. The Office Action cites *In re Aller*, 220 F2d 454,456, 105 USPQ 233, 235 (CCPA 1955) and MPEP § 2144.05 part II A for the proposition that in situations where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Applicants submit that the Office Action fails to set forth a *prima facie* case of obviousness because *In re Aller* does not apply to the presently claimed subject matter. In contrast to *In re Aller*, the subject matter of claim 1, as amended herein, is not merely selection of the optimum regimen from ranges previously disclosed in the prior art.

In each of the treatment cycles described in the art, the treatment days and rest days are dispersed as evenly as possible throughout the treatment cycle. In some of these treatment cycles (e.g., three days per week), some of the rest days must be consecutive, but the treatment days are dispersed nonconsecutively throughout the treatment cycle. In other described treatment cycles (e.g., five days per week), there must necessarily be consecutive treatment days, but the rest days are nonconsecutively dispersed throughout the treatment cycle.

The claimed treatment cycle represents an *entirely new* way of thinking about treatment cycles. This is made evident by the Commentary of Dr. Geisse in Kagy *et al.* cited in the Office Action. Dr. Geisse states: "What remains to be defined is the optimal dosing in which there can be three variables: concentration, the frequency of application, and the duration of the course of therapy." Thus, Dr. Geisse, one clearly skilled in the art, states that the obvious variables to explore for optimizing dosing by routine experimentation determine (a) how much drug is administered, (b) how often it is administered (e.g., once, twice, three times, five times, etc. per week), and (c) how long to provide treatment. Applicants have recognized a new variable: the *timing* of application throughout the treatment cycle. In the absence of hindsight derived from Applicants' disclosure, one skilled in the art would not have been motivated to modify the timing of administration within known treatment cycles to arrive at the claimed subject matter.

Even if, for the sake of discussion, the claimed subject matter is considered to be optimization from within a prior art range, obviousness is rebutted by data provided in Applicants' disclosure. MPEP § 2144.05 part III states: "Applicant can rebut a presumption of obviousness based on a claimed invention that falls within a prior art range by showing "(1) [t]hat the prior art taught away from the claimed invention...or (2) that there are new and unexpected results relative to the prior art." *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir. 2004)."

Applicants' submit that the efficacy of the claimed treatment cycle, demonstrated in Fig. 1 and Fig. 2, is an unexpected result: five consecutive days of treatment and two consecutive days of rest provides a response rate that is equal to or better than treatment seven days per week. Again Dr. Geisse's commentary in Kagy *et al.* supports Applicants' position. Dr. Geisse states, "As to frequency of application, our work clearly demonstrated dose-dependent effects particularly in terms of local adverse reactions." In other words, more frequent application

provided greater response rate and more local adverse effects. Less frequent application provided less severe adverse effects, but a decreased response rate. The claimed treatment cycle, in contrast, provides reduced adverse side effects compared to seven days of treatment per week, but without any dose-dependent reduction in response rate. This result is wholly unexpected relative to the prior art and expectations of those skilled in the art.

In summary, Applicants submit that the claimed treatment cycle is nonobvious over Beutner *et al.* and Kagy *et al.* because the claimed treatment cycle is not taught or suggested by the prior art and is not merely an optimization of ranges provided in the prior art. Moreover, the claimed treatment cycle provides an unexpected result relative to the prior art.

The rejection of claims 1, 7-12, and 16 under 35 USC § 103(a) as being unpatentable over Marks *et al.* or Beutner *et al.* or Kagy *et al.* or Geisse *et al.* has been overcome and should be withdrawn.

Claims 13-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Marks *et al.*, Beutner *et al.*, Kagy *et al.*, Geisse *et al.* in view of ALDARA (FDA Labeling Revision 2001). The FDA Labeling Revision is dated after the invention was made, as demonstrated by the Exhibit I and Exhibit II to the Affidavit of Mary L. Owens. The reference, therefore, is not prior art to the claimed subject matter and can not be used to cure the deficiencies of Marks *et al.*, Beutner *et al.*, Kagy *et al.*, or Geisse *et al.* to reject the claims under 35 U.S.C. § 103(a). Because each of claims 13-15 depend, ultimately, from claim 1, they are patentable over the cited primary references for at least all of the reasons set forth above regarding the rejection of claims 1-16 under 35 U.S.C. § 102(a) and the rejection of claims 1-12 and 16 under 35 U.S.C. § 103(a).

Claims 1-9 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dogan *et al.* Claims 2-6 have been canceled, so that remarks that follow pertain to claims 1 and 7-9.

Dogan teaches treatment of BCC by intralesional injection of IFN-α-2a three times per week for four weeks. The Office Action asserts that Dogan *et al.* sets forth the general conditions of the claimed method so that, under *In re Aller*, the claimed method is mere routine optimization of the ranges et forth in Dogan *et al.* Applicants respectfully traverse the rejection.

Applicants submit that Dogan *et al.* fails to set forth the general conditions of the claimed method—Dogan *et al.* fails to describe the IRM compound, a suitable range of concentrations of the IRM compound, and the route of administration recited in the claimed method—so that reliance on *In re Aller* is misplaced. Therefore, Applicants submit that the claimed subject matter is patentable over Dogan *et al.* for at least all of the reasons, set forth above, that the claimed subject matter is patentable over Buetner *et al.* and Kagy *et al.*

Thus, Applicants submit that the claimed treatment cycle is nonobvious over Dogan *et al.* because the claimed treatment cycle is not taught or suggested by, and is not merely an optimization of ranges provided in, Dogan *et al.*

The rejection of claims 1, 7-9 under 35 USC § 103(a) as being unpatentable over Dogan *et al.* has been overcome and should be withdrawn.

CONCLUSION

In view of the above, it is submitted that the application is in condition for allowance. Reconsideration of the application is requested.

Allowance of claims 1 and 7-16, as amended, at an early date is solicited.

Respectfully submitted,

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Date

By: Christopher D. Gram
Christopher D. Gram, Reg. No.: 43,643
Telephone No.: 651-733-1507

Office of Intellectual Property Counsel
3M Innovative Properties Company
Facsimile No.: 651-736-3833